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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,318	10/03/2001	Dominic E. Cosgrove	249.0002 0101	1885

26813 7590 08/10/2004

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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/970,318	COSGROVE, DOMINIC E.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *24-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/16/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I in the reply filed on May 21, 2004 is acknowledged.

2. With respect to applicant's arguments that the claims of group II are so interrelated with group I that no undue burden would be placed on examiner, the argument is found persuasive, and the restriction with regard to group II is withdrawn.

3. With respect to applicant's arguments regarding groups III and IV that the restriction would place an undue burden on applicant to pay for the costs for prosecuting 4 applications and maintaining 4 patents, it is believed that the withdrawal of the restriction between groups I and II would alleviate this burden, and the argument is not found persuasive. Since groups III and IV are distinct and independent inventions, and examining the additional groups would place an undue burden on examiner, the restriction regarding groups III and IV is maintained.

4. The requirement with regard to groups III and IV is still deemed proper and is therefore made FINAL.

Response to Amendment

5. Applicant's amendment of claims 1, 2, 8 and 15 is acknowledged.

6. Claims 1-41 are currently pending.

7. Claims 24-41 are withdrawn.

Information Disclosure Statement

8. The unconsidered reference in the IDS has now been considered. The copy of the reference was greatly appreciated.

Rejections Withdrawn

9. Applicant's arguments, see pages 11-17, filed May 21, 2004, with respect to the rejections under 35 U.S.C. 112, second paragraph, and 35 U.S.C. 103 have been fully considered and are persuasive. The rejections of claims 1-7, 15-23 have been withdrawn.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In claims 1, 8, and 15, applicant recites antibodies immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4. In the specification, however, applicant has only disclosed antibodies immunoreactive with SEQ ID NOs: 1, 2, and 4, and has only provided working examples of antibodies immunoreactive with SEQ ID

NOs: 1 and 2. However, different antibodies would be capable of being immunoreactive with portions of the human usherin protein, and not be immunoreactive with SEQ ID NOs: 1 and 2.

12. Claims 1, 8, 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not reasonably provide enablement for a method of determining whether an individual is at risk for developing Usher syndrome Type IIa.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 1, 8, and 15 are broadly drawn to a method comprising the step of incubating a biological sample with any antibody immunoreactive with a portion of a protein having SEQ ID NO: 4.

Applicant, however, does not specify what portion and how large of a portion of the human usherin protein with which the antibody is immunoreactive, nor does applicant teach the specificity the antibody toward the portion of the protein with which it is

immunoreactive. According to Eudy et al [Eudy et al, Molecular genetics of Usher syndrome, 1999, Cell Mol Life Sci, 56, 258-267], the USH2A protein shares 32% identity and 47% similarity between residues 300 and 1050 with all laminin family members (p. 263, col.1). Eudy et al further teach that the USH2A protein contains LE repeats and F3 repeats, which are common to other extracellular proteins and cell adhesion molecules as well (p.263, col.1). Therefore, antibodies immunoreactive with the LE or F3 regions of the usherin protein would also be immunoreactive with other extracellular matrix proteins and cell adhesion molecules, thus generating false negatives.

Although applicant states that the antibodies preferably selectively recognize the usherin protein epitopes and bind to these epitopes with high affinity (p. 16, lines 25-30), applicant fails to specify any epitopes, nor does the applicant teach how to create antibodies that would be capable of binding to the epitopes in the protein with high affinity, rendering it unclear how a person of ordinary skill in the art would be able to do so. Furthermore, in the claims, applicant merely requires that an antibody that is immunoreactive with a portion of a human usherin protein, and does not limit the antibodies to specific epitopes or regions of the protein.

In the specification, applicant further states that the methods of the present invention also provide for the use of antibodies that are immunoreactive with an usherin protein encoded by the USH2A gene, as well as other polypeptides (16, lines 22-25). If the antibody forms an immunoconjugate with other polypeptides, false negatives would potentially be generated, as immunoconjugates would be present even though the usherin protein is not.

Furthermore, applicant teaches that there is likely some percentage of individuals with Usher syndrome Type IIa that continue to express immunoreactive usherin in their tissues (p.15, lines 9-16). Applicant, however, has not specified what percentage of individuals would continue to do so, rendering it unclear what the accuracy of the method and level of predictability would be in determining whether an individual would have or be at risk for developing Usher syndrome Type IIa.

While applicant does provide working examples of antibodies immunoreactive with SEQ ID NOs: 1 and 2 (p. 22, example 1), it is unclear the specificity of the antibodies toward the sequences, and if the antibodies selectivity recognize the usherin protein epitopes, and where the epitopes are. In addition, applicant does not provide any data involving the use of the antibodies in tissue samples from individuals with Usher syndrome Type IIa, rendering it unclear how well the antibodies would perform in determining individuals having or being at risk for Usher syndrome Type IIa.

As applicant has pointed out, previous results have also suggested that usherin might have very restricted tissue distribution (p.37, lines 25-30) (p.1755, cols. 1-3, [Eudy et al, Mutation of a gene encoding a protiein with extracellular matrix motifs in usher syndrome type IIa, 1998, Science, 280, 1753-1757]). While applicant teaches that usherin is expressed in the basement membranes of a large number of tissues in mice (p. 38, lines 3-10), applicant has only established that usherin is associated with the basement membranes of the retina in humans (p. 38, lines 28-30). Furthermore, applicant does not show the distribution or detection of usherin, in samples in the diseased state, from individuals having Usher syndrome Type IIa. Applicant also fails to recite that the tissue samples include basement membranes in the claims, which would potentially result in

false positives, if the portion of tissue used as the biological sample does not contain basement membranes.

The specification does not teach a method of determining whether an individual has or is at risk for developing Usher syndrome type IIa using antibodies that bind only a portion of a human usherin protein having SEQ ID NO:4. Insufficient direction or guidance and no working examples are provided to assist one skilled in the art to make and use antibodies to perform a method of determining whether an individual is at risk for developing Usher syndrome Type IIa as recited in claims 1-23.

Response to Arguments

13. Applicant's arguments with respect to claims 1, 15, have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

15. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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